spastic paraplegia type 31

Spastic paraplegia type 31 is one of a group of genetic disorders known as hereditary spastic paraplegias. These disorders are characterized by progressive muscle stiffness (spasticity) and the development of paralysis of the lower limbs (paraplegia) caused by degeneration of nerve cells (neurons) that trigger muscle movement. Hereditary spastic paraplegias are divided into two types: pure and complicated. The pure types involve only the lower limbs, while the complicated types also involve the upper limbs and other areas of the body, including the brain. Spastic paraplegia type 31 is usually a pure hereditary spastic paraplegia, although a few complicated cases have been reported.

The first signs and symptoms of spastic paraplegia type 31 usually appear before age 20 or after age 30. An early feature is difficulty walking due to spasticity and weakness, which typically affect both legs equally. People with spastic paraplegia type 31 can also experience progressive muscle wasting (amyotrophy) in the lower limbs, exaggerated reflexes (hyperreflexia), a decreased ability to feel vibrations, reduced bladder control, and high-arched feet (pes cavus). As the condition progresses, some individuals require walking support.

Frequency

Spastic paraplegia type 31 is one of a subgroup of hereditary spastic paraplegias known as autosomal dominant hereditary spastic paraplegia, which has an estimated prevalence of one to 12 per 100,000 individuals. Spastic paraplegia type 31 accounts for 3 to 9 percent of all autosomal dominant hereditary spastic paraplegia cases.

Genetic Changes

Spastic paraplegia type 31 is caused by mutations in the *REEP1* gene. This gene provides instructions for making a protein called receptor expression-enhancing protein 1 (REEP1), which is found in neurons in the brain and spinal cord. The REEP1 protein is located within cell compartments called mitochondria, which are the energy-producing centers in cells, and the endoplasmic reticulum, which helps with protein processing and transport. The REEP1 protein plays a role in regulating the size of the endoplasmic reticulum and determining how many proteins it can process. The function of the REEP1 protein in the mitochondria is unknown.

REEP1 gene mutations that cause spastic paraplegia type 31 result in a short, nonfunctional protein that is usually broken down quickly. As a result, there is a reduction in functional REEP1 protein. It is unclear how *REEP1* gene mutations lead to the signs and symptoms of spastic paraplegia type 31. Researchers have shown that mitochondria in cells of affected individuals are less able to produce energy, which may

contribute to the death of neurons and lead to the progressive movement problems of spastic paraplegia type 31; however, the exact mechanism that causes this condition is unknown.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- autosomal dominant spastic paraplegia 31
- spastic paraplegia 31
- SPG31

Diagnosis & Management

These resources address the diagnosis or management of spastic paraplegia type 31:

- GeneReview: Hereditary Spastic Paraplegia Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1509
- Genetic Testing Registry: Spastic paraplegia 31, autosomal dominant
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1853247/
- Spastic Paraplegia Foundation, Inc.: Treatments and Therapies
  http://sp-foundation.org/understanding-pls-hsp/treatments.html

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Health Topic: Neurologic Diseases
  https://medlineplus.gov/neurologicdiseases.html
- Health Topic: Neuromuscular Disorders
  https://medlineplus.gov/neuromusculardisorders.html
- Health Topic: Paralysis
  https://medlineplus.gov/paralysis.html

Genetic and Rare Diseases Information Center

- Hereditary spastic paraplegia
  https://rarediseases.info.nih.gov/diseases/6637/hereditary-spastic-paraplegia

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Hereditary Spastic Paraplegia Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Hereditary-spastic-paraplegia-Information-Page

Educational Resources

- Disease InfoSearch: Spastic paraplegia 31, autosomal dominant
  http://www.diseaseinfosearch.org/Spastic+paraplegia+31%2C+autosomal+dominant/9319
- MalaCards: spastic paraplegia 31
  http://www.malacards.org/card/spastic_paraplegia_31
- National Health Service (UK)
  http://www.nhs.uk/Conditions/spastic-paraplegia/Pages/Introduction.aspx
- Orphanet: Autosomal dominant spastic paraplegia type 31
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=101011
- Orphanet: Hereditary spastic paraplegia
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=685
- The Merck Manual Home Edition: Hereditary Spastic Paraparesis
  http://www.merckmanuals.com/home/brain-spinal-cord-and-nerve-disorders/spinal-cord-disorders/hereditary-spastic-paraparesis
- Washington University, St. Louis: Neuromuscular Disease Center
  http://neuromuscular.wustl.edu/spinal/fsp.html#spg31

Patient Support and Advocacy Resources

- Contact a Family (UK)
  http://www.cafamily.org.uk/medical-information/conditions/f/familial-spastic-paraplegia/
- National Organization for Rare Disorders (NORD): Hereditary Spastic Paraplegia
  https://rarediseases.org/rare-diseases/hereditary-spastic-paraplegia/
- RareConnect
  https://www.rareconnect.org/en/community/hereditary-spastic-paraplegia
- Resource List from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/hsp.html
- Spastic Paraplegia Foundation, Inc.
  http://sp-foundation.org/understanding-pls-hsp/hsp.html

GeneReviews

- Hereditary Spastic Paraplegia Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1509

Genetic Testing Registry

- Spastic paraplegia 31, autosomal dominant
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1853247/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22spastic+paraplegia+type+31%22+OR+%22SPG31%22+OR+%22Spastic+Paraplegia%2C+Hereditary%22+OR+%22spastic+paraplegia+31%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28SPG31%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- SPASTIC PARAPLEGIA 31, AUTOSOMAL DOMINANT
  http://omim.org/entry/610250

Sources for This Summary

- Beetz C, Schüle R, Deconinck T, Tran-Viet KN, Zhu H, Kremer BP, Frints SG, van Zelst-Stams WA, Byrne P, Otto S, Nygren AO, Baets J, Smets K, Ceulemans B, Dan B, Nagan N, Kassubek J, Klimpe S, Klopstock T, Stolze H, Smeets HJ, Schrander-Stumpel CT, Hutchinson M, van de Warrenburg BP, Braastad C, Deufel T, Pericak-Vance M, Schöls L, de Jonghe P, Züchner S. REEP1 mutation spectrum and genotype/phenotype correlation in hereditary spastic paraplegia type 31. Brain. 2008 Apr;131(Pt 4):1078-86. doi: 10.1093/brain/awn026. Epub 2008 Mar 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18321925
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2841798/
- Goizet C, Depienne C, Benard G, Boukhris A, Mundwiller E, Solé G, Coupry I, Pilliod J, Martin-Négrier ML, Fedirko E, Forlani S, Cazeneuve C, Hannequin D, Charles P, Feki I, Pinel JF, Ouvrard-Hernandez AM, Lyonnet S, Ollagnon-Roman E, Yaouanq J, Toutain A, Dussert C, Fontaine B, Leguern E, Lacombe D, Durr A, Rossignol R, Brice A, Stevanin G. REEP1 mutations in SPG31: frequency, mutational spectrum, and potential association with mitochondrial morpho-functional dysfunction. Hum Mutat. 2011 Oct;32(10):1118-27. doi: 10.1002/humu.21542. Epub 2011 Sep 9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21618648
- Hewamadduma C, McDermott C, Kirby J, Grierson A, Panayi M, Dalton A, Rajabally Y, Shaw P. New pedigrees and novel mutation expand the phenotype of REEP1-associated hereditary spastic paraplegia (HSP). Neurogenetics. 2009 Apr;10(2):105-10. doi: 10.1007/s10048-008-0163-z. Epub 2008 Nov 26.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19034539
- Züchner S, Wang G, Tran-Viet KN, Nance MA, Gaskell PC, Vance JM, Ashley-Koch AE, Pericak-Vance MA. Mutations in the novel mitochondrial protein REEP1 cause hereditary spastic paraplegia type 31. Am J Hum Genet. 2006 Aug;79(2):365-9. Epub 2006 May 26.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16826527
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1559498/

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/spastic-paraplegia-type-31

Reviewed: April 2015
Published: February 7, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services